

FIG. 1A

1 GTCTTCACCATGCATCGCTGGGCTTCTTCTGTGTGGGTGTCTCTCTGTCGCCGCTG 60
 CAGGAAGTGTGCTACCTGAGCGACCCGAAGAAGAGACACCGCACAGAGACGAGCGCGAC
 M H S L G F F S V A C S L L A A A -
 61 CGGTGCTCCCGGTCTCGCGAGGCGCGCGCGCGCGCGCTTCGAGTCCGGACTCG 120
 GCGACGAGGCGCCAGAGCGCTCCGCGGGCGCGCGCGCGGAGCTCAGGCCCTGAGC
 L L P G P R E A P A A A A A F E S G L D -
 121 ACCTCTCGGACGCGGAGCCCGACGCGGGGAGGCGCACGGCTTATGCAAGCAAGATCTGG 180
 TGGAGAGCTGCGCTCGGGCTGCGCCGCTCCGGTGCCGAATACGTTCTGTTCTAGACC
 L S D A E P D A G E A T A Y A S K D L E -
 240 AGGAGCAGTTACGGTCTGTGTCTCCAGTGTAGATGAACATCATGACTGTACTTACCCAGAAT 240
 TCCTCGTCAATGCCAGACACAGGTACATCTACTTGAAGTACTGACATGAGATGGGTCTTA
 E Q L R S V S S V D E L M T V L Y P E Y -
 241 ATTGGAAATGTACAAGTGTACGTAAGGAAAGAGGCTGGCAACATAACAGAGAACAGG 300
 TAACCTTTTACATGTTACAGTCGATTCCTTCTCCCGACCGTTGTTGTTCTCTTCTCC
 W K M Y K C Q L R K G G W Q H N R E Q A -
 CCAACCTCAACTCAAGGACAGAAGAGACTATAAATTTGCTGACGACACATTATATATACAG

MATCH WITH FIG. 1B

FIG. 1B

MATCH WITH FIG. 1A

301 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 360
 GGTGGAGTTGAGTCCCTGCTCTCTGATATTTTAAACGACGTCGTGTAATATTATGTC
 N L N S R T E E T I K F A A A H Y N T E -
 C

361 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 420
 AGATCTTGAAAGTATTGATAATGAGTGGAGAAAGACTCAATGTCATGCCAGGGAGGTGT
 TCTAGAACTTTTCATAACTATTACTCACTCTTTCTGAGTTACGTACGGTGCCCTCCACA
 I L K S I D N E W R K T Q C M P R E V C -
 C

421 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 480
 GTATAGATGTGGGAAGGAGTTTGGAGTCGCGACAAACACTTCTTTAAACCTCCATGTG
 CATATCTACACCCCTTCTCAAACCTCAGCGCTGTTGTGGAAGAAATTTGGAGGTACAC
 I D V G K E F G V A T N T F F K P P C V -
 C

481 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 540
 TGTCCGTCTACAGATGTGGGGGTGCTGCAATAGTAGAGGGGCTGCAGTGCATGAACACCA
 ACAGGCAGATGTCTACACCCCAAGCAGTATCTACTCCCGACGTCACGTACTTGTGTT
 S V Y R C G C C N S E G L Q C M N T S -
 C

541 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 600
 GCACGAGTACCTCAGCAAGACGTTATTTTGAAATTACAGTGCCTCTCTCTCAAGGCCCA
 CGTGTCTGAGTGGAGTCGTTCTGCAATAAAGTTTAACTTAACTGTCACGGAGAGAGAGTTCGGGGT
 T S Y L S K T L F E I T V P L S Q G P K -
 C

601 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 660
 AACAGTAACAATCAGTTTTGCCAATCACACTTCTCTGCCGATGCATGCTTAAACGTGATG
 TTGTGCATTGTAGTCAAAACGGTTAGTGTGAAGGAGGGTACGTACAGATTTGAOCTAC
 P V T I S F A N H T S C R C M S K L D V -
 C

MATCH WITH FIG. 1C

FIG. 1C

MATCH WITH FIG. 1B

661 TTTACAGACAAGTTCATTCCATTATTAGACGTTCCCTGCCAGCAACACTACCACAGTGTCTC
 AAATGCTGTTCAAGTAAGGTAATAATCTGCAAGGACGGTCTGTGTGATGGTGTACACAG
 Y R Q V H S I I R R S L P A T L P Q C Q -
 AGCAGCGACACAGACCTGCCCCACCAATTACATGTGGAAATAATCACATCTGCAGATGCC
 721 TCCGTCGCTGTCTTGGACGGGGTGGTAAATGTAACAQCTTATTAGTGTAGACGCTTACGG
 A A N K T C P T N Y M N N H I C R C L -
 TGGCTCAGGAAGATTTTATGTTTTCTCGGATGCTGGAGATGACTCAACAGATGGATTCC
 781 ACCGATCTCTTCTAAATAACAAAAGGAGCCTACGACCTCTACTGAGTTGTCTACCTAAGG
 A Q E D F M F S S D A G D D S T D G F H -
 ATGACATCTGTGGACCAACAAAGGAGCTGGATGAAGAGACCTGTCTAGTGTCTCTGCAGAG
 841 TACTGTAGACACCTGGTTTGTCTCGACCTTACTCTCTGGACAGTCACACAGACGCTCTC
 D I C G P N K E L D E T C C Q C V C R A -
 CGGGCTTCGGCCTGCCAGCTGTGGACCCCAAGAACTAGACAGAACTCATGCCAGT
 901 GCCCGAAGCCGGACGCTCGACACCTGGGGTCTTCTTGAATCTGTCTTGAATACGCTCA
 G L R P A S C G P H K E L D R N S C Q C -
 GTGTCTGTAAACAAACTCTTCCCGAGCCCAATGTGGGGCCCAACCGAGAAATTTGATGAAA
 1020 CACAGACATTTTGTGTGAGAAGGGGTCGGTACACCCGGTGGTCTTAACTACTTT
 MATCH WITH FIG. 1D

MATCH WITH FIG. 1D

U

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1  CGAGGCCACGGCTTATGCAAGCAAAGATCTGGAGGAGCAGTTACGGTCTGTGTCCAGTGT
   - - - - - + - - - - - + - - - - - + - - - - - + - - - - - + - - - - - +
71  AGATGAATTCATGACTGTACTCTACCCAGAATATTGGAATAATGTACAAGTGTCAAGTAAG
   - - - - - + - - - - - + - - - - - + - - - - - + - - - - - + - - - - - +
      M T V L Y P E Y W K M Y K C Q L R
121  GAAAGGAGGTGGCAACATAACAGAGAACAGGCCAACCTCAACTCAAGCACAGAAGAGAC
   - - - - - + - - - - - + - - - - - + - - - - - + - - - - - + - - - - - +
      K G G W Q H N R E Q A N L N S R T E E T
181  TATAAAATTTGCTGCAGCACATTATAATACAGAGATCTTGAAAAGTATTGATAATGAGTG
   - - - - - + - - - - - + - - - - - + - - - - - + - - - - - + - - - - - +
      I K F A A A H Y N T E I L K S I D N E W
241  GAGAAAGACTCAATGCATGCCACGGGAGGTGTGTATAGATGTGGGGAAGGAGTTTGGAGT
   - - - - - + - - - - - + - - - - - + - - - - - + - - - - - + - - - - - +
      R K T Q C M P R E V C I D V G K E F G V
301  CCGGACAAACACCTTCTTTAAACCTCCATGTGTGTCCGTCTACAGATGTGGGGTGTGCTG
   - - - - - + - - - - - + - - - - - + - - - - - + - - - - - + - - - - - +
      A T N T F F F K P P C V S V Y R C G G C C

```

FIG. 2A

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361 CAATAGTGAGGGCTGCAGTGCATGAACACCAGCAGCAGCTACCTCAGCAGACAGCTTATT
-----+-----+-----+-----+-----+-----+-----+-----+
N S E G L Q C M N T S T S Y L S K T L F

421 TGAATACAGTGCCTCTCTCAAGGCCCCAACACAGTAACAATCAGTTTGGCAATCA
-----+-----+-----+-----+-----+-----+-----+-----+
E I T V P L S Q G P K P V T I S F A N H

481 CACTTCCTGCCGATGCATGCTAAACTGGATGTTTACACACAAGTTCATTCCATTATTAG
-----+-----+-----+-----+-----+-----+-----+-----+
T S C R C M S K L D V Y R Q V H S I I R

541 ACGTTCCCTGCCAGCAACACTACCACAGTGTGAGGAGGAGCAAGACCTGCCCCACCAA
-----+-----+-----+-----+-----+-----+-----+-----+
R S L P A T L P Q C Q A A N K T C P T N

601 TTACATGTGGAATAATCACATCTGCAGATGCCTGGCTCAGGAAGATTTATGTTTCCCTC
-----+-----+-----+-----+-----+-----+-----+-----+
Y M W N N H I C R C L A Q E D F M F S S

661 GGATGCTGGAGATGACTCAACAGATGGATTCCATGACATCTGTGGACCAACAAGGAGCT
-----+-----+-----+-----+-----+-----+-----+-----+
D A G D D S T D G F H D I C G P N K E L

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FIG.2B

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721  GGATGAAGAGACCTGTCACTGTCTGCAGAGCGGGGCTTCGGCCTGCCAGCTGTGGACC
      D E E T C C Q C V C R A G L R P A S C G P
      CCACAAAGAACTAGACAGAACTCATGCCAGTGTGTCTGTAAACAACTCTTCCCCAG
      H K E L D R N S C Q C V C K N K L F P S
      CCAATGTGGGCGCAACCGAGAAATTGATGAAACACATGCCAGTGTGTATGTAAAGAAGC
      Q C G A N R E F D E N T C Q C V C K R T
      CTGCCCCAGAAATCAACCCCTAAATCCTGGAAATGTGCCTGTGAATGTACAGAAAGTCC
      C P R N Q P L N P G K C A C E C T E S P
      ACAGAAATGCTTGTAAAGGAAGAAAGTTCCACCACCAACATGCAGCTGTACAGACG
      Q K C L L K G K K F H H Q T C S C Y R R
      GCCATGTACGAACCGCCAGAGGCTTGTGAGCCAGGATTTTCATATAGTGAAGAAGTGTG
      P C T N R Q K A C E P G F S Y S E E V C

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FIG.2C

1081	TCGTTGTGTCCTTCATATATTGGCAAGACCACAAATGAGCTAAGATTGTACTGTTTTCCA
	R C V P S Y W Q R P Q M S
1141	GTTCAATCGATTTCATTATATGGAAACCTGCTGCCACAGTAGAAGCTGTCTGTGAACAGA
1201	GAGACCCCTGTGGGTCCATGCTAACAAAGACAAAGCTGTCTCTTTCCCTGAACCATGTGGA
1261	TAACTTTACAGAAATGGACTGGAGCTCATCTGCAGGCTCTTTGTAAGAGACTGGTTTT
1321	CTGCCAATGACCAACAGCCCAAGATTTTCCCTCTGTGATTCTTTAAAGAATGACTATA
1381	TAATTATTTCACATAAAATATTGTTCTCTGCATTCATTTTTTATAGCAACAACAATTGGT
1441	AAACTCACTGTGATCAATATTTTTTATATCATGCAAAAATATGTTTAAATAAATAATGAAAA
1501	TTGTATTATAAAAAAAAAAAAAA

FIG. 2D

50

1

pdgfa .MRTLACLLL LGGYLAVL AEEAEIPREV IERLARSQIH SIRDLORLLE
 pdgfb MNRCWA.LFL SLCCYLRLVS AEGDPIPEEL YEMLSHSHIR SFDDLQRLH
 VegfMNFL SWVHSLALL LY..... .LHAKWSQA
 Vegf2MTV LYPEYWKMYK CQ..... .LRKGWQHEN

100

51

pdgfa IDSVGSEDSL DTSIRAHGVH ATKHVPEKRP LPTRKRSI.EEAVP
 pdgfb GDP.GEEDGA ELDLNMTRSH SGELES... .LARGRRSLG SLTIAEPAMI
 Vegf APMAE..... GGGQ NHHEVVKFMD .VYQR.....
 Vegf2 REQANLNSRT EETIKFAAAH YNTEILKSID NEWRK.....

150

101

pdgfa AVCKTRTVLY EIPRSQVDPT SANFLWPPC VEVRCTGCC NTSSVKCPQS
 pdgfb ABCKTRTEVF ETSRLIDRT NANFLWPPC VEVRCSGCC NNRNVQCRPT
 Vegf SYCHPIETLV DIFQEPDEI ..EYIFKPS C VPLMRGGCC NDEGLECVPT
 Vegf2 TQCMPEVCI DVGKEFGVAT ..NTFFKPPC VSVRCGGCC NSEGLQCMNT

200

151

pdgfa RVHRSVKVA KVEYVRKKPK LKEVQVRLEE HLECRAC.... AT.....
 pdgfb QVQLRPVQVR KIEIVRKKPI FKKATVLED HLACKC.... ETVAARPVT
 Vegf EESNITWQIM RIK.PH..QG QHIGEMSFLQ HNKCECRPKK DRARQEKKS
 Vegf2 STSYLSKTLF EIT.VELSQG PKPVTISFAN HTSCRCMSKL DVYRQVHSII

FIG. 3A

201					250
Pdgfa	TSLNPD	YREEDTDVR.
Pdgfb	RSPGGSQEQR	AKTPQTRVTI	RTVRVRPPK	GKRRKFKHTH	DKTALKETLG
Vegf	RGK.....	.GKGQKRRK	KSRYKSWSY	VGARCCLMFW	SLPGPHP...
Vegf2	RRSLPATLPQ	QQAANKTCPT	NYMWNHICR	CLAQEDFMFS	SDAGDDSTDG
251					300
Pdgfa
Pdgfb	A.....
Vegf	CGP...	CSE	RRKHLFVQDP
Vegf2	FHDICGNKE	LDEETCQCVC	RAGLRPASC	G	PHKEL...DR
					NSCQCVCNKK
301					350
Pdgfa
Pdgfb
Vegf	..	DSRCKARQ	LELNERTCRC	DKPRR
Vegf2	LFPSQCGANR	EFDENTCQC	VCKRTCPRNQ	PLNPGKCACE	CTESPQKCLL
351					398
Pdgfa
Pdgfb
Vegf
Vegf2	KGKKFHHQTC	SCYRRPCPTR	QKACEPGFSY	SEEVCRCVPS	YWQRPQMS

FIG. 3B

PERCENTAGE (%) OF AMINO ACID IDENTITIES BETWEEN EACH PAIR OF GENES IS SHOWN IN THE FOLLOWING TABLE				
	PDGF α	PDGF β	VEGF	VEGF2
PDGF α				
PDGF β	48.0			
VEGF	20.7	22.7		
VEGF2	23.5	22.4	30.0	

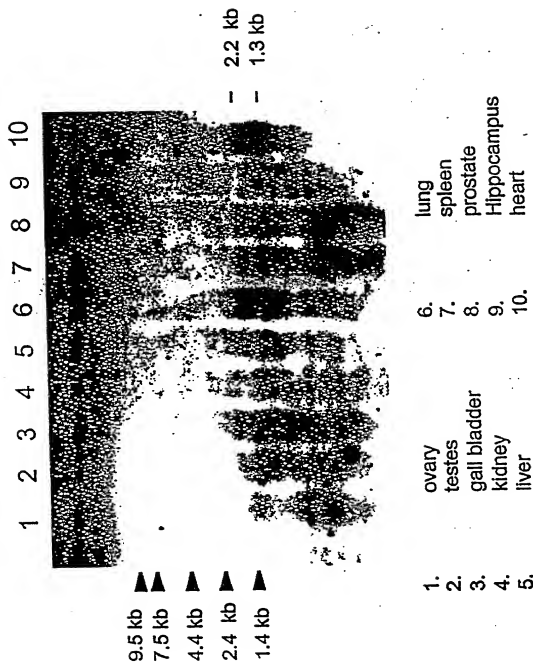
FIG. 4

Expression of VEGF2 mRNA in
Human Breast Tumor Cells



1. normal breast tissue
2. breast tumor tissue
- 3-9. breast tumor cell lines.

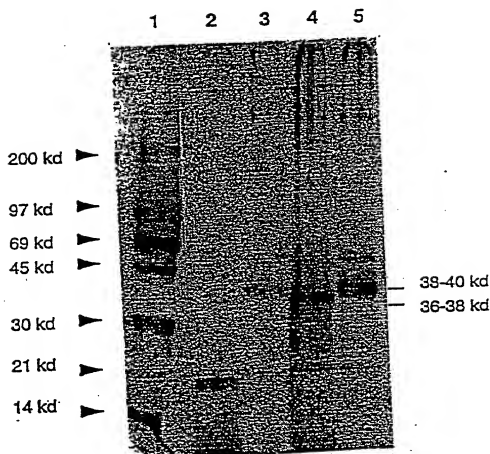
FIG. 5



Expression of VEGF2 mRNA in human adult tissues.

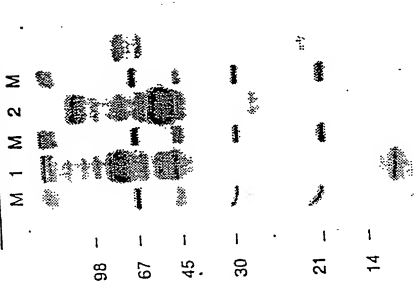
FIG. 6

FIG. 7



Lane 1: 14-C and rainbow M.W. marker
 Lane 2: FGF control
 Lane 3: VEGF2 (M13-reverse & forward primers)
 Lane 4: VEGF2 (M13-reverse & VEGF-F4 primers)
 Lane 5: VEGF2 (M13-reverse & VEGF-F5 primers)

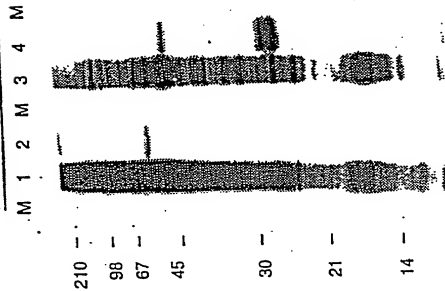
non-reducing gel



Lane M: Marker
Lane 1: vector medium
Lane 2: VEGF2 medium

FIG. 8A

reducing gel



Lane M: Marker
Lane 1: vector cytoplasm
Lane 2: vector medium
Lane 3: VEGF2 cytoplasm
Lane 4: VEGF2 medium

FIG. 8B

FIG. 9



Lane 1: Molecular weight marker
Lane 2: Precipitates containing VEGF2.

FIG. 10

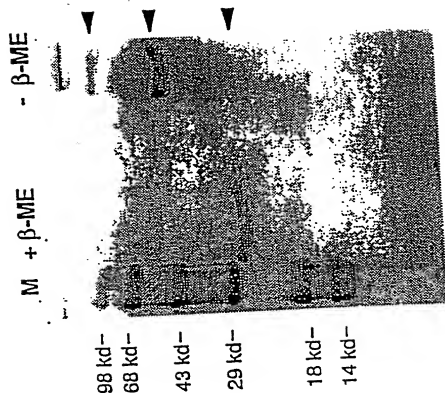


FIG. 11

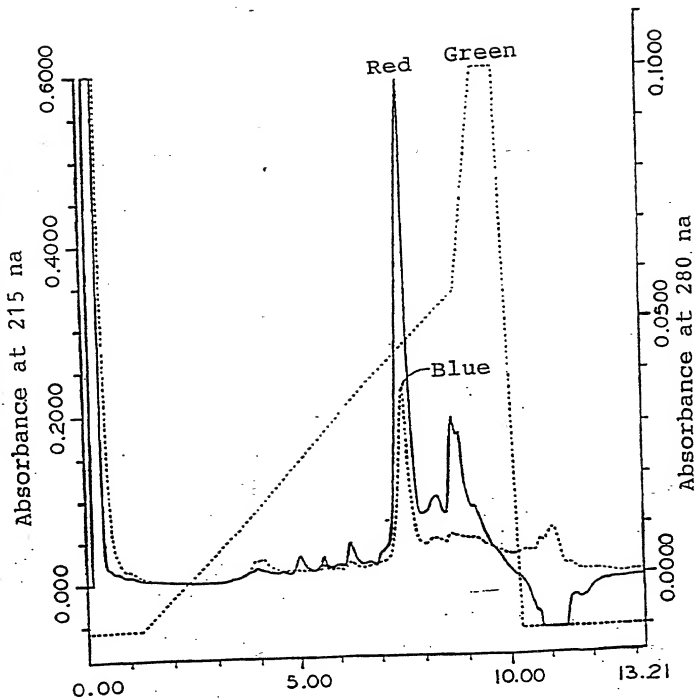


FIG. 12

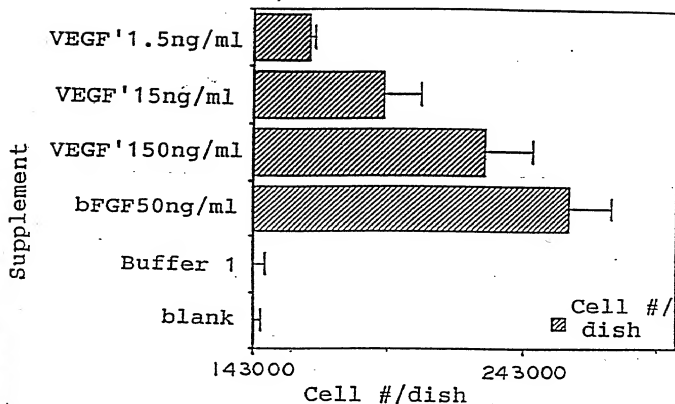
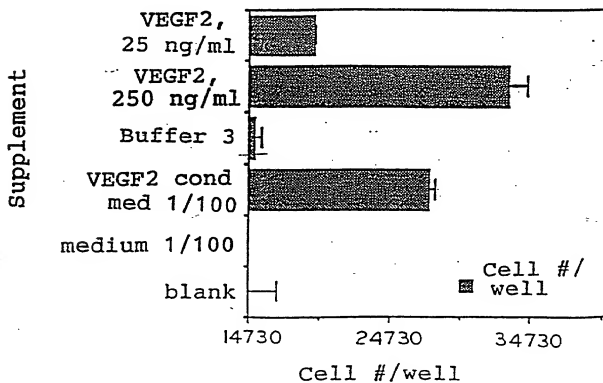


FIG. 13



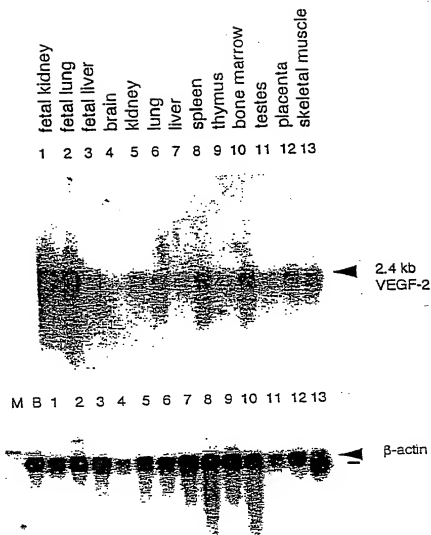
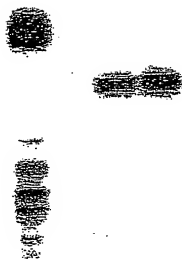


Figure 14

1 2 3 4 5 6

2.4 kb



1. Molecular Weight Marker
2. umbelical vein endothelial cells
3. aortic smooth muscle cells
4. Dermal fibroblast

Figure 15

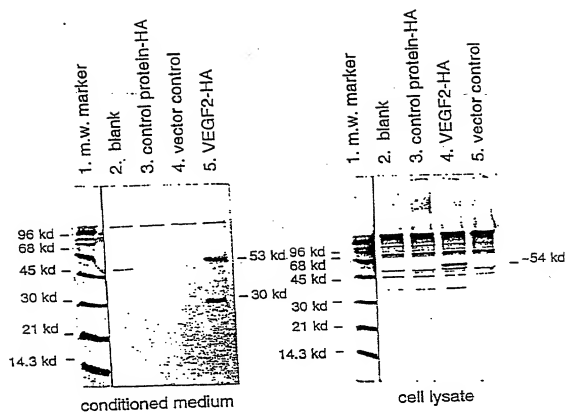


Figure 16

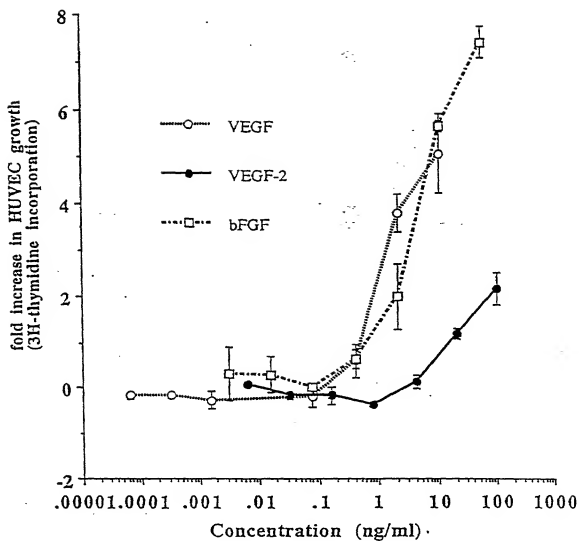


Figure 17

104280-9245663

Fluorescence

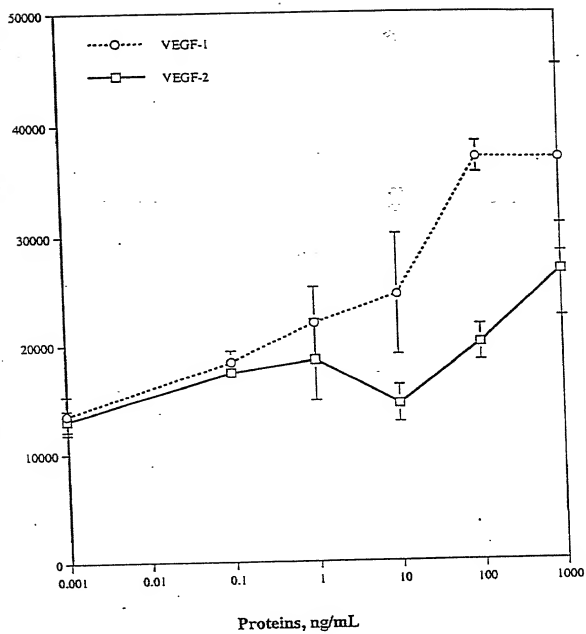


Figure 18

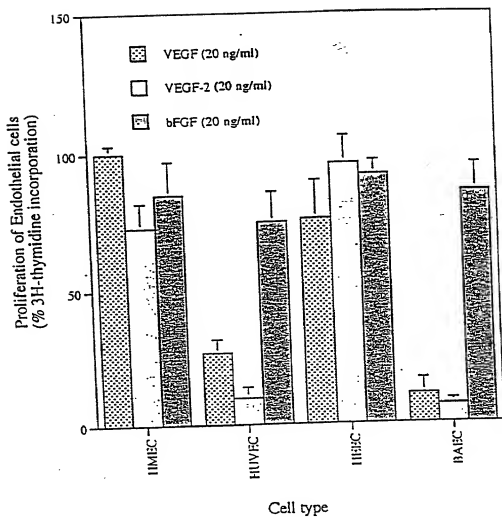
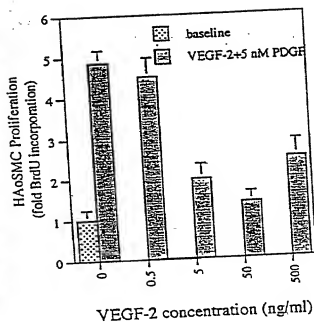


Figure 19

A.



B.

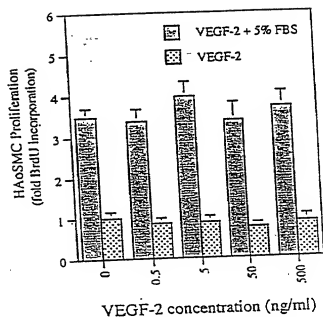


Figure 20

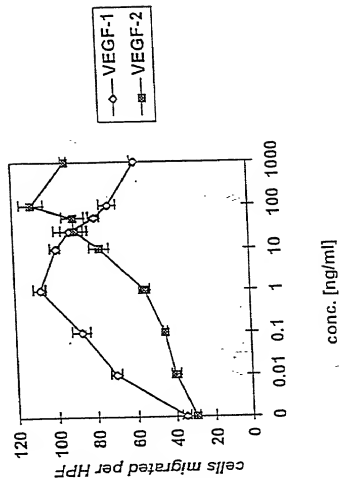
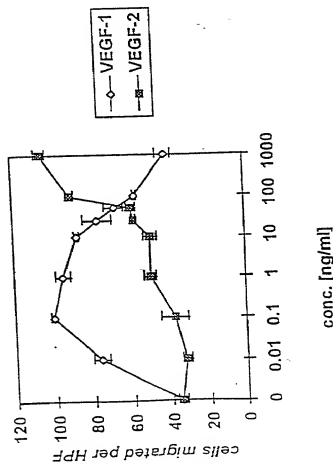
BMEC MigrationHUVEC Migration

Figure 21

HUVEC - NO-Release

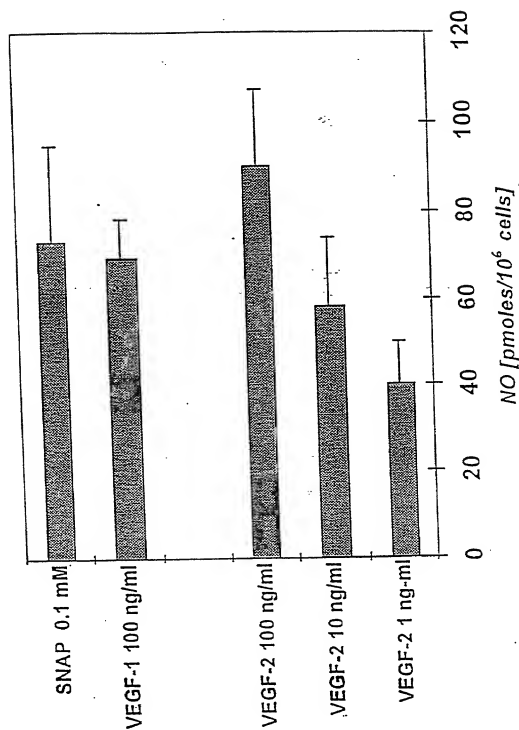


Figure 22

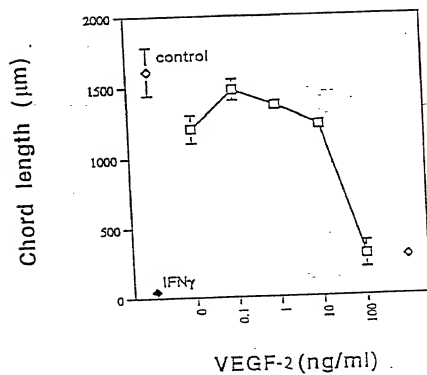


Figure 23

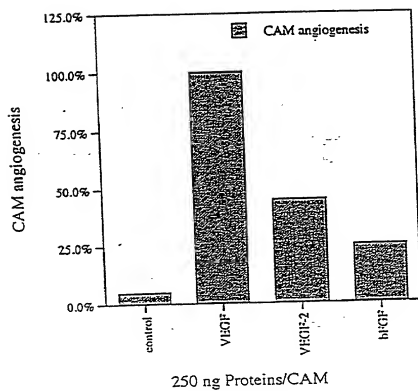
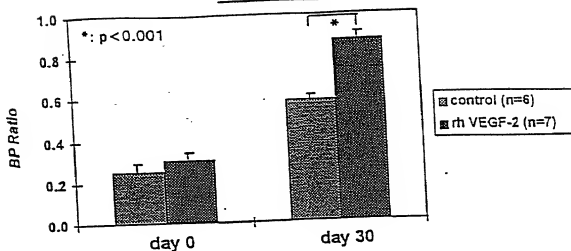
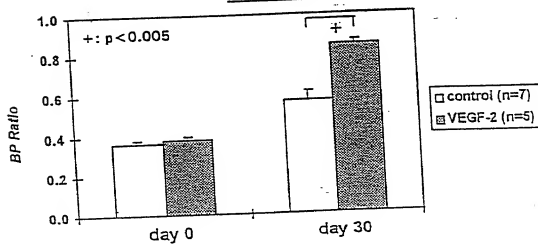


Figure 24

Calf Blood Pressure Ratio
- Protein i.a. -



Calf Blood Pressure Ratio
- Plasmid -



Calf Blood Pressure Ratio

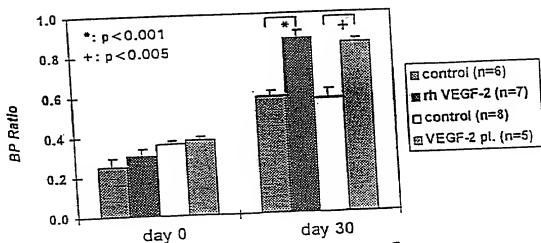


Figure 25A

00935726-00000000

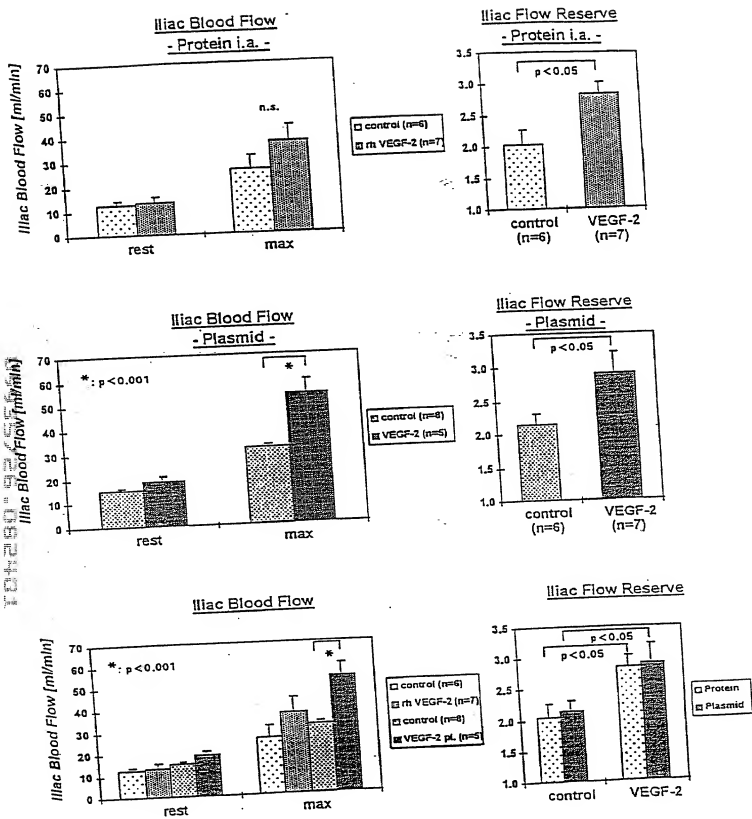
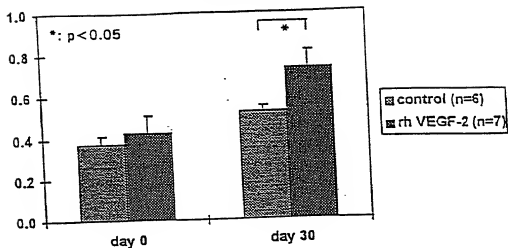
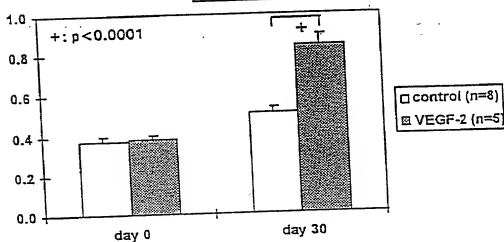


Figure 25B

Angiographic Score
- Protein i.a. -



Angiographic Score
- Plasmid -



Angiographic Score

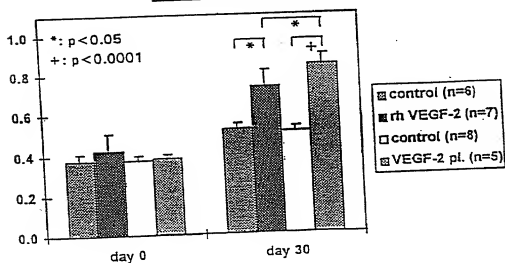
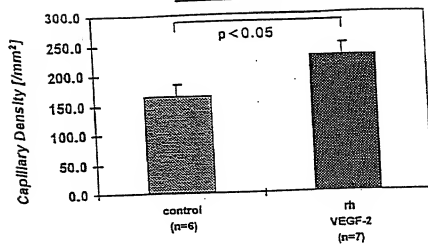


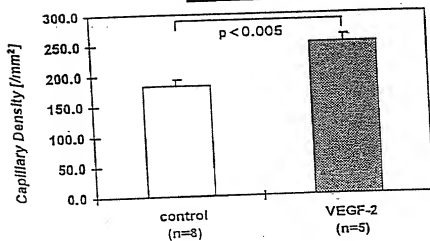
Figure 25C

0935766-082401
104280-925560

Capillary Density
- Protein i.a. -



Capillary Density
- Plasmid -



Capillary Density

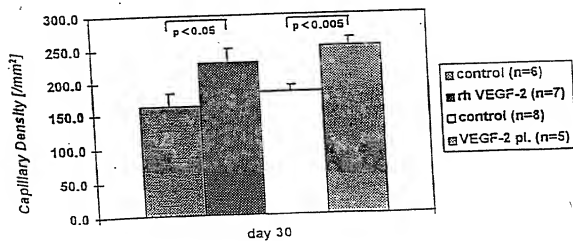
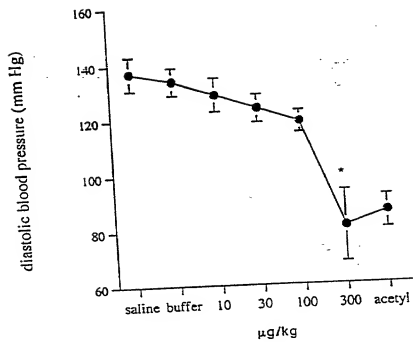


Figure 25D

**Figure 26A**

0935726-08244
101280-92/55660

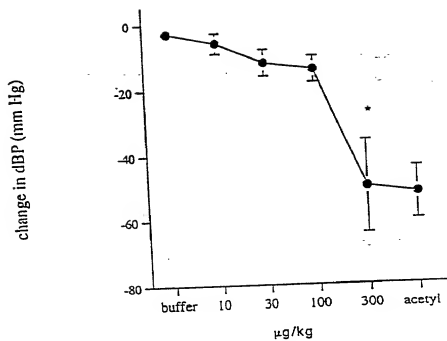


Figure 26B

104220-0245660

MAP (mm Hg)

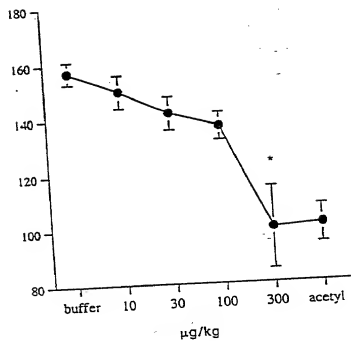
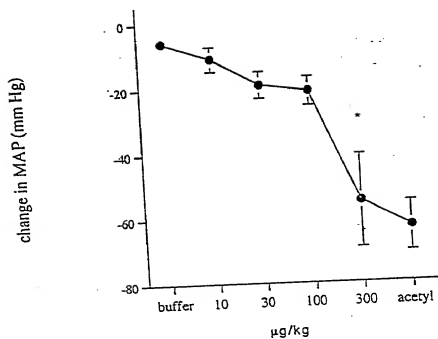
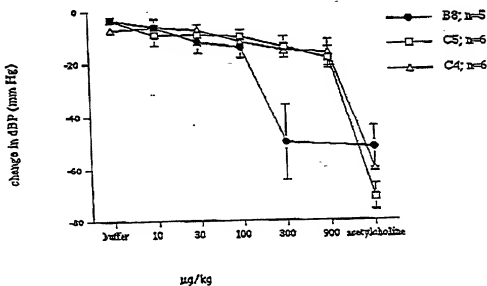


Figure 26C

**Figure 26D**

Change in diastolic blood pressure of SHR rats given increasing doses of VEGF-2

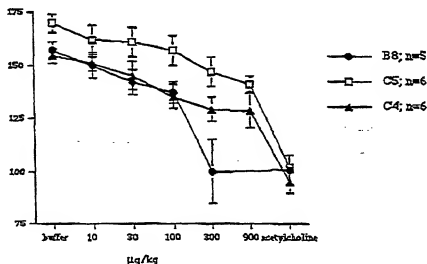


Increasing doses of VEGF-2 (HG00403-B8, HG00404-C5, and HG00404-C4) were administered to 13-14 week old SHR (spontaneously hypertensive rats) and the data are expressed as the mean \pm SEM. Statistical analysis was performed with a paired t-test and significance was defined as $p < 0.05$ vs. the response to buffer alone. The response to B8 and C4 were significant at the 300 μ g/kg dose. The response to C5 was significant at the 100, 300, and 900 μ g/kg doses.

The effect of increasing doses of VEGF-2 on the mean arterial pressure (MAP) of SHR rats

Figure 26E

The effect of increasing doses of VEGF-2 on the mean arterial pressure (MAP) of SHR rats

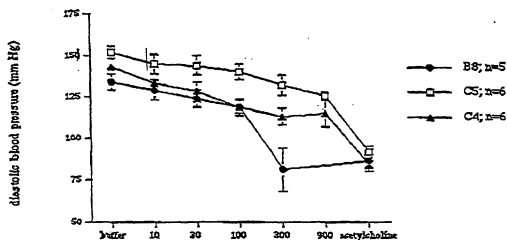


Increasing doses of VEGF-2 (HG00403-B8, HG00404-C5, and HG00404-C4) were administered to 13-14 week old SHR (spontaneously hypertensive rats) and the data are expressed as the mean \pm SEM. Statistical analysis was performed with a paired t-test and significance defined as $p < 0.05$ vs. the response to buffer alone. The response to B8 was significant at a 300ng/kg dose. Administration of C5 yielded significant responses at doses greater than or equal to 100 ng/kg. The response to C4 was significant when 10, 100, 300, and 900 ng/kg were given.

The effect of VEGF-2 on the diastolic blood pressure of SHR rats

Figure 26F

The effect of VEGF-2 on the diastolic blood pressure of SHR rats



Increasing doses of VEGF-2 (HG00403-B8, HG00404-CS, HG00404-C4) were administered to 13-14 week old SHR (spontaneously hypertensive rats) and the data are expressed as the mean \pm SEM. Statistical analysis was performed with a paired t-test and statistical significance was defined as $p < 0.05$ vs. the response to buffer alone. The response to B8 was significant only at the 300 μ g/kg dose and when given acetylcholine. The responses to C4 and CS, while much less dramatic, were statistically significant at all dose levels.

Figure 26G

VEGF2N.ck

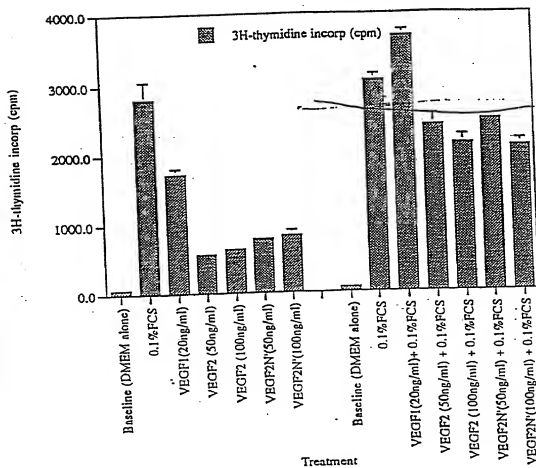


Figure 27

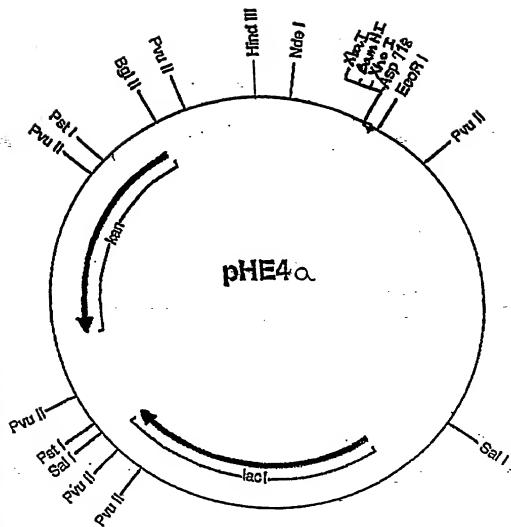


Figure 28

Figure 29

1 AAGCTTAAAAAACTGCAAAAATAGT TTGACT Operator 1
-35

50 TAAGATGTACCCA Operator 2
-10 TTACACATTAA

S/D
94 A GAGGAGAAATTA CATATG